Women's Health Initiative Overview

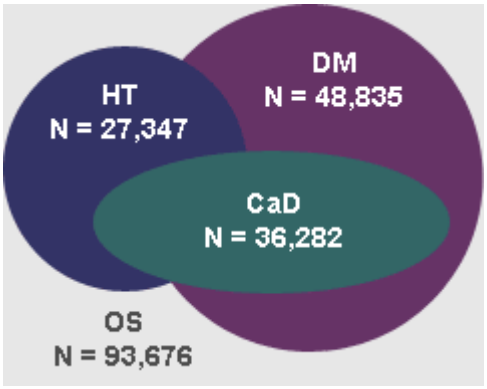
The Women's Health Initiative (WHI) was a long-term national health study that focused on strategies for preventing heart disease, breast and colorectal cancer and osteoporosis in postmenopausal women. These chronic diseases are the major causes of death, disability and frailty in older women of all races and socioeconomic backgrounds.

This multi-million dollar, 15-year project, sponsored by the National Institutes of Health (NIH), National Heart, Lung, and Blood Institute (NHLBI), involved over 161,000 women aged 50-79, and was one of the most definitive, far reaching clinical trials of women's health ever undertaken in the U.S. The WHI Clinical Trial and Observational Study attempted to address many of the inequities in women's health research and provide practical information to women and their physicians about hormone replacement therapy, dietary patterns and calcium/vitamin D supplements, and their effects on the prevention of heart disease, cancer and osteoporosis.

The WHI Clinical Trial and Observational Study were conducted by 40 Clinical Centers in 24 states and the District of Columbia. The Fred Hutchinson Cancer Research Center in Seattle, WA served as the WHI Clinical Coordinating Center for data collection, management, and analysis.

The WHI study had three components: a randomized clinical trial, an observational study and a community prevention study.

The WHI Clinical Trials (CT) (N=68,132) included three overlapping components, each a randomized controlled comparison among women who were postmenopausal and aged 50-79 at randomization. The three CT components were:



- **Hormone Therapy (HT)**: This component examined the effect of HT on the prevention of heart disease and osteoporosis, and any associated risk for breast cancer. Women in the HT were randomized within one of two double-blind trials, Estrogen plus Progestin or Estrogen-Alone, depending on hysterectomy status at baseline. In the Estrogen plus Progestin trial, 16,608 women with an intact uterus at baseline were randomized 1:1 to take either combined Estrogen plus Progestin or placebo study pills. In the Estrogen-Alone trial, 10,739 women who were post-hysterectomy at baseline were randomized 1:1 to take either unopposed estrogen or placebo.

- **Dietary Modification (DM)**: This component evaluated the effect of a low-fat, high fruit, vegetable and grain diet on the prevention of breast and colorectal cancer and heart disease. The 48,835 women who joined the DM were randomly assigned to either a sustained low-fat eating pattern (40% of the women) or their usual, self-selected dietary behavior (60%). Women joining the DM could be randomized in groups of 2 to 8 women in special circumstances, such as when they lived and prepared meals together.

- **Calcium/Vitamin D (CaD)**: This component evaluated the effect of calcium and vitamin D supplementation on the prevention of osteoporosis-related fractures and colorectal cancer. Women participating in either DM or HT were invited to join the CaD trial 12 to 24 months after randomization. The 36,282 women eligible for the double-blind CaD trial were randomized 1:1 to take study pills containing calcium/vitamin D or a placebo.

Eligible women could be randomized into one, two, or all three of the CT components. Women who were ineligible or unwilling to join the CT were invited to join the **Observational Study (OS)** (N=93,676). The Observational Study (OS) examined the relationship between lifestyle, health and risk factors and specific disease outcomes.

Age distribution goals were specified for the CT as follows: 10% for ages 50-54; 20% for ages 55-59; 45% for ages 60-69; 25% for ages 70-79. Another study goal was to enroll women of racial/ethnic minority groups in the same proportion as found in the general population, according to the 1990 census.

Eligibility was defined generally for all WHI components with component-specific exclusion criteria. At the time of enrollment, all women were required to be between 50 and 79 years old, postmenopausal, and intending to reside in the area for at least 3 years.

Recruitment began in September 1993 and continued through December 1998. Women interested in joining the WHI were initially screened by telephone to determine basic eligibility, followed by up to three baseline screening visits to complete the following: 1) physical measurements (height, weight, blood pressure, heart rate, waist and hip circumference), 2) collection of blood specimens (stored as serum, plasma, and buffy coat), 3) a medication / supplement inventory; and 4) questionnaires on demographic characteristics, medical history, family history, reproductive history, lifestyle/behavioral factors, and quality of life. During screening, women received information about the WHI components, and additional procedures were conducted to assess eligibility (including breast exams, food records for the Dietary Modification Trial, and a pelvic exam with endometrial aspiration and a placebo run-in for the Hormone Therapy Trials). At the end of the recruitment period, 161,808 women had joined the WHI, with about 17% representing racial/ethnic minority groups.

The **community prevention study (CPS)** was a unique collaborative venture between the Centers for Disease Control and Prevention (CDC), and the National Institutes of Health. Eight University-based Prevention Centers underwritten by CDC conducted and evaluated health programs that encouraged women of all races and socioeconomic backgrounds to adopt healthful behaviors such as improved diet, nutritional supplementation, smoking cessation, exercise and early detection of treatable health problems. The goal of the community prevention study was to develop carefully evaluated, model programs that could be implemented in a wide range of communities throughout the U.S.